UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,692	08/26/2006	Rajiv Nayar	ARR-0037-1 US	3669

77845 7590 03/04/2009

Goodwin Procter LLP
Attn: Patent Administrator
135 Commonwealth Drive
Menlo Park, CA 94025-1105

EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
03/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,692	NAYAR ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment of October 10, 2008, in response to the action of April 10, 2008, is acknowledged. It is acknowledged that applicants have amended Claim 1. Claims 1-21 are pending, are directed to a single invention drawn to a dry powder composition comprising recombinant human alpha 1-antitrypsin, and are reconsidered.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

Provisional rejection of Claims 1-21 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over Claims 1-3, 6, 8, 9, 12, 29, 31, and 32 of US 10/579,088 for the reasons explained in the prior action, is maintained. Applicants did not comment on this rejection.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of Claims 13 and 14, under 35 U.S.C. 112, second paragraph, because the phrase "equivalent to" renders the claim indefinite, is withdrawn for the following reasons. In support of their request that said rejection be withdrawn, Applicants argue that the skilled artisan would know that an Arrhenius analysis can be used to determine the temperature/time dependence for inactivation of a polypeptide. This argument is found to be persuasive in light of

Yu et al, 1988, which teaches methods for Arrhenius analysis to determine the temperature/time dependence for inactivation of recombinant α1-antitrypsin (pg 801, parg 1; Fig 3). Therefore, rejection of Claims 13 and 14, under 35 U.S.C. 112, second paragraph, because the phrase "equivalent to" renders the claim indefinite, is withdrawn.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 1-21 under 35 U.S.C. 112, first paragraph/lack of enablement, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

The present specification need not disclose any structural or functional details regarding recombinant human α1-antitrypsin because this information was well-known to those of ordinary skill in the art at the time of filing, for reasons set forth in (A)-(C).

(A) The specification provides that rAAT "is a 395 amino acid protein of 44 kD, that is non-glycosylated and has an amino acid sequence identical to the human plasma protein (AAT) with the exception of an N-acetylmethionine residue at the amino terminus" (lines 6-10, page 1).

(B) US 5,780,014 ("014 patent"), incorporated by reference into Applicant's application, discloses that α1-antitrypsin is "a protease inhibitor with inhibitory activity toward neutrophil elastase." (Col 1, lines 22-23). The '014 patent further specifies the source of alpha-1 antitrypsin (Col. 3, lines 32-40).

US 5,780,014 incorporates by reference US 4,599,311 ("311 patent"). The '311 patent provides the genomic location and amino acid sequence of human alpha 1-antitrysin (Col. 6, 11.17-19; Col. 7-10). The '311 patent also provides for a recombinant human alpha 1- antitrypsin that employs a yeast host and explains that the resulting polypeptide differs in degree of glycosylation from naturally occurring human alpha 1-antitrypsin (Col. 11, 11.18-29).

(C) Travis et al. (1985) J. Biol. Chem. 260:4384-4389 ("Travis et al.") provide experimental procedures for isolating human recombinant AAT and studying its molecular properties, including protocols for testing the proteinase inhibitory activity of rAAT polypeptides.

(D) A person of ordinary skill in the art would understand "non- glycosylated recombinant human alpha 1-antitrypsin" to have its ordinary meaning, i.e., a protease inhibitor with inhibitory activity toward neutrophil elastase (Col 1, lines 22-23 of the '014 patent) having the amino acid sequence shown in Col. 7-10 of the '311 patent.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that the specification so discloses. However, said disclosure is not sufficient to enable the skilled artisan to make and use any human polypeptide having any α1-antitrypsin activity.

(B) Reply: It is acknowledged that US 5,780,014 discloses that α1-antitrypsin is "a protease inhibitor with inhibitory activity toward neutrophil elastase" and that some forms of α1-antitrypsin are commercially available. However, said disclosure is not sufficient to enable the skilled artisan to make and use any human polypeptide having any α1-antitrypsin activity. Also, see (D), below.

It is acknowledged that US 5,780,014 incorporates by reference US 4,599,311 and that US 4,599,311 discloses the sequence of a human α1-antitrypsin polypeptide. However, the incorporation by reference of US 4,599,311 into US 5,780,014 does not, by right, constitute incorporation by reference of US 4,599,311 into the instant Application (Rule 1.57). Even if incorporation by reference of US 4,599,311 into US 5,780,014 did constitute incorporation by reference of US 4,599,311 into the instant Application, which it currently does not, said incorporation does not disclose that the α1-antitrypsin polypeptide disclose by US 4,599,311 is the same as the polypeptide used in the instant Application. Moreover, the single α1-antitrypsin polypeptide disclose by US 4,599,311 does not enable skilled artisan to make and use the genus of any human polypeptide having any α1-antitrypsin activity. Searching the sequence databases, using BLAST, with the α1-antitrypsin polypeptide disclose by US 4,599,311 did not identify said polypeptide but identifies over 100 polypeptides having as low as 64% identity with the polypeptide of US 4,599,311 and annotated as "α1-antitrypsin"; many said identified polypeptides have not been demonstrated to have any α1-antitrypsin activity. Thus, the skilled artisan would not be enabled for making and using any human polypeptide having any α1-antitrypsin activity.

(C) Reply: Travis et al fails to disclose any recombinant α1-antitrypsin protein or the sequence of any α1-antitrypsin protein. Travis et al fails to enable the full scope of the recited invention.

(D) Reply: A person of ordinary skill in the art would not understand recombinant human α1-antitrypsin to mean the protease inhibitor having the amino acid sequence shown in Col. 7-10 of the '311 patent and having inhibitory activity toward neutrophil elastase because: (i)

the skilled artisan would know that α1-antitrypsins have activity against trypsin, chymotrypsin, anionic trypsin, chymotrypsin II, pancreatic elastases, granulocytic elastase, and acrosin (Pannell et al, 1974), as well as neutrophil elastase and, more likely than not other proteases, (ii) as explained above, there are a wide variety of structural proteins annotated as having α1-antitrypsin activity, and (iii) there are a variety of mutated human α1-antitrypsin proteins (Mulgrew et al, 2007, review),

For these reasons and those explained in the prior action, rejection of Claims 1-21 under 35 U.S.C. 112, first paragraph/enablement, is maintained.

Written Description

Rejection of Claims 1-21 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) Applicants submit that the invention, the nature of the written description rejection, and the legal analysis in the Capon and Falkner decisions are analogous to those of the present case. Applicants submit that in the instant application, (i) the claims are directed to a novel dry powder composition comprising non-glycosylated recombinant human α1-antitrypsin; (ii) the Examiner has failed to consider the state of scientific knowledge; (iii) the Examiner has improperly applied a per se rule requiring recitation in the specification of the structural details or amino acid sequences, when those sequences are already known in the field, and (iv) the Examiner has failed to properly consider the generic concept of the Applicants' invention.

(A) Reply: These arguments are not found to be persuasive for the following reasons.

(i) It is acknowledged that the claims are directed to a dry powder composition comprising non-glycosylated recombinant human α1-antitrypsin.

(ii) As explained above, the state of the art is that the structure and function of all α1-antitrypsin proteins were not known at the priority date of the instant Application.

(iii) See (ii).

(iv) The Examiner understands that Applicants believe that the generic concept of their invention is the formulation of a protein (human α1-antitrypsin) in a dry powder. Nonetheless, all limitations of the claims must be described in either the specification or the prior art in a manner such that the skilled artisan would recognize that Applicants were in possession of their recited invention. Neither the specification nor the prior art describe the structure or function of all human α1-antitrypsin proteins.

For these reasons and those explained in the prior action, rejection of Claims 1-21 under 35 U.S.C. 112, first paragraph/written description, is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of Claims 1-19 and 21 are rejected under 35 U.S.C. 102(b), as being anticipated by Eljamal et al, 1998, for the reasons explained in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following argument. Claim 1 recites a dry powder composition comprising non-glycosylated

recombinant human α1-antitrypsin. By contrast, Eljamal et al discloses that "purified human plasma αlAT was supplied by Armour Pharmaceutical Co." was used to make a powder composition (Col. 10, lines 38-52; Example 1) limiting the reference to natural AAT, which is known to be glycosylated.

This argument is not found to be persuasive because, as explained in the prior action, Eljamal et al teach that recombinant forms of α1-antitrypsin can be used in their method (col 3, parg 5). For these reasons and those explained in the prior action, rejection of Claims 1-19 and 21 under 35 U.S.C. 102(b), is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claim 20 under 35 U.S.C. 103(a) as being unpatentable over Eljamal et al, 1998 in view of Millqvist-Fureby et al, 1999, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) Eljamal et al does not teach use of a recombinant or a non-glycosylated α1-antitrypsin polypeptide and Millqvist-Fureby et al does not remedy the deficiency of Eljamal et al.

(B) Travis et al. (1985) discloses that the stabilization of rAAT is more difficult than stabilization of natural AAT; with rAAT having a half-life that is considerably less than that of natural AAT (p. 4338).

These arguments are not found to be persuasive for the following reasons.

(A) Reply: See the reasons stated above, under 35 U.S.C. 102(b).

(B) Reply: It is Eljamal et al that teaches use of a recombinant/ non-glycosylated α1-antitrypsin polypeptide. Millqvist-Fureby et al teach addition of a surfactant to the composition, which would stabilize both the isolated and the recombinant α1-antitrypsin polypeptides.

For these reasons and those explained in the prior action, rejection of Claim 20 under 35 U.S.C. 103(a), is maintained.

Allowable Subject Matter

No claims are allowable.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Any new references were cited solely to support rejection(s) based on amendment or rebut Applicants' arguments. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-092834. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652